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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/749,532	YAMAKAWA ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *7/11/08 and 4/23/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,10-12,15-18 and 37-43* is/are pending in the application.

4a) Of the above claim(s) *40-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,10-12,15-18 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's request for reconsideration of the finality of the rejection of the last Office action in the telephonic interview between the Examiner and Mr. Martin Sulsky on April 23, 2008 is persuasive and, therefore, the finality of that action is withdrawn. The rejections are as follows:

Newly submitted claims 40-43 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: new claim 40 comprises distinct process step of associating a biomolecule with the identified peptide with any of the different types of nanocode bound to the biomolecule. Furthermore, new claim 43 recites numerous distinct species that have not been claimed or examined before.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 40-43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of Claims

Claims 1, 4-7, 10-12, 15-18 and 37-43 are pending.

Claims 40-43 are withdrawn from consideration as being directed to a non-elected invention.

Claims 1, 4-7, 10-12, 15-18 and 37-39 are under examination.

Withdrawn Rejection

In view of the amendments to the claims the 35 USC 112, first paragraph (new matter) and second paragraph (in-part) rejections are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7, 10-12, 15-18 and 37-39, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record as reiterated below.

Written Description Rejection

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

The specification fails to provide an adequate written description for a method for identifying a peptide that binds to a surface of a material having a flat surface. The disclosure fails to disclose any peptide that has been identified from a phage display library that binds to any kind or type of surface material having a flat surface. Furthermore, the disclosure does not disclose fabrication of a biosensor with the identified peptide. The description in the disclosure for each of the huge components use in the methods is provided only in terms of its definitions. It does not describe the kind of a material that has a flat surface or the surface to which the known phage library binds. A listing of **definition** of every possible surface material or biosensor does not constitute a written description of every species in a genus of a material on a surface or biosensor with a nanocode. It would not "reasonably lead" those skilled in the art to any particular species. In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967). Particularly since the disclosure does not describe or exemplify a single species of the genus components. To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention. Applicants are further referred to the CAFC decision in the

University of California vs. Eli Lilly and Co. CAFC 43 USPQ2d 1398 7/22/1997 with respect to adequate disclosure of the scope of the presently claimed method. Adequate disclosure, like enablement, requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See In re Riat (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr. (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University of California v. Eli Lilly and Co. (for disclosure).

Response to Arguments

Applicants note that independent claim 1 was amended in the previous response to replace "exposing a known phage library to a surface of a material having specific geometric patterns specific geometric patterns" with "exposing a known phage library to a surface of a material having a flat surface." Thus, the Examiner rejects a feature that is no longer in the claim, rendering the rejection moot.

In reply, please see the rejection above, as applied to the amended claims.

Applicants further note that support for binding phages to a flat surface can be found in paragraphs [0012], [0017],

[0030], and [0035]. Additionally, Applicants note that Belcher (US 2003/0113714) teaches attaching peptides to HOPG, a smooth, flat surface in Example III (paragraphs [0127]). To satisfy the written description requirement, the specification need only describe in detail that which is new or not conventional. See Hybritech v. Monoclonal Antibodies, 802 F.2d 1367, 1384 (Fed. Cir. 1986). Fonar Corp. v. General Electric Co., 107 F.3d 1543, (Fed. Cir. 1997).

In reply, a review of the cited sections above, e.g., paragraph [0017] reveal nothing more than, again definitions of the different terms as claimed. Applicants' arguments as to the specification need only describe in detail that which is new or not conventional is unclear. As stated above neither the specification nor the claims describe what is considered novel. The claims recite a known phage display library and as stated by applicants above the material, as described by Belcher,(not by the disclosure), is also known. If everything is conventional, as alleged, then the disclosure must have produced or identified at least a peptide that binds to a surface with any material which is a flat surface. In the absence of such description, the written description requirement has not been satisfied.

New Matter Rejection

Claim 1, as amended, drawn a method of exposing a phage library to a surface of a material is not supported in the as-filed specification. The as-filed specification does not recite broadly a material without the target. Hence, the broad claimed material on a surface would include a huge scope of materials, organic or inorganic, not originally disclosed in the as-filed specification.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-7, 10-12, 15-19 and 37-39, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained only for the claims as reiterated immediately below.

B). The term "specific" in claim 1 is a relative term which renders the claim indefinite. The term is not defined by the

claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to the basis by which a material of a flat surface is based upon given no structure or name for said material of a flat surface. It is not clear as to the qualifying features of said surface material.

Response to Arguments

Applicants amended claim 1 to replace "specific geometric patterns" with "flat surface." Applicant submits that this rejection is moot. Further, regarding the phrase "a peptide that demonstrates specific binding to the flat surface" in step (f), Applicants note that "specific binding" is described in paragraph [0032] of the specification: [0032] Accordingly, methods of the present invention involve the use of phage display technology to identify, through combinatorial directed evolution, specific amino acid sequence(s) of a peptide that preferentially bind to a specific material surface of a geometrically distinct structure, such as a substrate for a measurement devices or analytical instrument that utilize substrates of particular shapes or atomic configuration, such as scanning probe microscopy (SPM).

In reply, amending the claims to a flat surface does not obviate this rejection as it is unclear how a peptide of unknown constitution can specifically bind to a flat surface also of unknown make-up. As clearly stated by applicants above, **specific amino acid sequences** of a peptide preferentially bind to a **specific material surface** of a flat surface. None of the claims recites any specific amino acid sequences or material surface.

In view of the cancellation of claims 2 and 19 and amendments to claims 15 and 19, the 35 USC 112, second paragraph rejection in the last Office action is withdrawn.

The newly amended claims 1, 4-7, 10-12, 15-18 and 37-39, are rejected as follows;

1. In claim 1 the step of "fabricating a biosensor having a flat substrate and a peptides identified by step(f)" is unclear and does not seem to correspond to the preceding steps. It is unclear as to the essentially of fabricating a biosensor given that the peptide has already been identified and synthesized and confirmed without the need of a biosensor. Is the biosensor having a flat substrate the same or different from step (a) surface of a material having a flat surface? The term "flat" is a relative term. The standard or basis by which

said flat surface is compared relative thereto is not clearly set forth in the claims or specification.

2. Claim 15 is unclear since if it is a flat surface, how can it be curved? It is further unclear whether the surface is made up of boron nitrate and etc.

3. Claim 39 is unclear as to what constitutes a "desired feature" of the peptide? Does feature relates to a chemical, physical, biochemical or physico-chemical feature of a peptide?

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1, 4-7, 10, 16, 18, and 19, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Naik et al (Nature) for reasons of record as reiterated below.

Naik discloses at page 169, cols. 1 and 2 a method of identifying a silver binding peptides from a combinatorial phage display peptide library comprising contacting a phage display peptide library with a inorganic surface, as silver. Naik discloses at page 170 up to page 171 that the silver particles were analyzed by transmission electron microscope. The

examination of the silver nanoparticles obtained using AG4 peptide revealed the presence of hexagonal, spherical and triangular silver particles. The silver crystal exhibited a flat plate-like morphology. See further the Methods at page 172 which provide a detail description of the method. The broad claimed method utilizing broad components is fully met by the process of Naik using specific components therein.

Claims 1, 4-7, 10-12, 15 and 18-19, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Belcher (US 20030113714).

Belcher discloses in the abstract a method for selective binding of amino acid oligomers to semiconductor and elemental carbon-containing materials. Belcher discloses at [0047] that "elemental carbon-containing molecule" generally refers to allotropic forms of carbon. Examples include, but are not limited to, diamond, graphite and highly ordered pyrolytic graphite (HOPG). At paragraph [0048] the "substrate" may be a microfabricated solid surface to which molecules attach through either covalent or non-covalent bonds and includes, e.g., silicon, mica, gold, silver, metal, metal alloy and combinations thereof capable of having functional groups such as amino, carboxyl, thiol or hydroxyl incorporated on its surface. The

substrate may be porous, planar or nonplanar. The substrate includes a contacting surface that may be the substrate itself or a second layer (e.g., substrate or biologic material with a contacting surface) made of organic or inorganic molecules and to which organic or inorganic molecules may contact. Belcher discloses that previously it was shown that peptides may bind to semiconductor material. Semiconductor materials useful in binding peptides include, but are not limited to gallium arsenide, indium phosphate, gallium nitrate, zinc sulfide, aluminum arsenide, aluminum gallium arsenide, cadmium sulfide, cadmium selenide, zinc selenide, lead sulfide, boron nitride and silicon. At paragraph [0054] it was disclosed that the method provides a random organic polymer pool using a Phage-display library. A Phage-display library is a combinatorial library of random peptides containing between 7 and 12 amino acids fused to the pIII coat protein of M13 coliphage, providing different peptides that are reactive with crystalline semiconductor structures or other materials. At paragraph [0055] peptide sequences have been developed with affinities for various materials such as semiconductors, and elemental carbon-containing molecules such as graphite. At paragraph [0056] Belcher discloses that using a Phage-display library, protein sequences that successfully bound to the specific crystal were eluted from the surface, amplified

by, e.g., a million-fold, and reacted against the substrate under more stringent conditions. This procedure was repeated between ***three and seven times to select the phage in the library with the most specific binding peptides. After, e.g., the third, fourth and fifth rounds of phage selection, crystal-specific phage were isolated and their DNA sequenced, identifying the peptide binding that is selective for the crystal composition (for example, binding to GaAs but not to Si) and crystalline face (for example, binding to (100) GaAs, but not to (111)B GaAs).***

Response to Arguments

Applicants state that with the amendments to claim 1, none of the applied references teach the fabrication of a biosensor.

In response, the broad claim biosensor, which reads on a huge scope of materials, is anticipated by the prior art specific target. The target (biomolecule as claimed) binds and senses the presence of the peptide from the phage library, as disclosed by each of the cited references above.

Applicants'' attention is drawn, for example, to the Belcher's reference, which discloses at **e.g.**, paragraph:

> [0059] Phage, tagged with streptavidin-labeled 20-nm colloidal gold particles bound to the phage through a biotinylated antibody to the M13 coat protein, was used for quantitative assessment of specific binding. X-ray photoelectron spectroscopy (XPS) elemental composition determination was performed, monitoring the phage substrate interaction through

the intensity of the gold 4f-electron signal (FIGS. 2a-c). Without the presence of the G1-3 phage, XPS confirmed that the antibody and the gold streptavidin did not bind to the GaAs(100) substrate. The gold-streptavidin binding was, therefore, specific to the peptide expressed on the phage and an indicator of the phage binding to the substrate. Using XPS it was also found that the G1-3 sequence isolated from GaAs(100) bound specifically to GaAs(100) but not to Si(100) (see FIG. 2a). In a complementary fashion the S1 clone, screened against the (100) Si surface, showed poor binding to the (100) GaAs surface. [0059] Phage, tagged with streptavidin-labeled 20-nm colloidal gold particles bound to the phage through a biotinylated antibody to the M13 coat protein, was used for quantitative assessment of specific binding. X-ray photoelectron spectroscopy (XPS) elemental composition determination was performed, monitoring the phage substrate interaction through the intensity of the gold 4f-electron signal (FIGS. 2a-c). Without the presence of the G1-3 phage, XPS confirmed that the antibody and the gold streptavidin did not bind to the GaAs(100) substrate. The gold-streptavidin binding was, therefore, specific to the peptide expressed on the phage and an indicator of the phage binding to the substrate. Using XPS it was also found that the G1-3 sequence isolated from GaAs(100) bound specifically to GaAs(100) but not to Si(100) (see FIG. 2a). In a complementary fashion the S1 clone, screened against the (100) Si surface, showed poor binding to the (100) GaAs surface.

Attention is drawn to Naik which discloses at e.g., page 169, col. 2:

The phages expressing peptides that exhibited selective affinity for silver. after several rounds ofpannin8, were eluted from the surface of the silver particles and re-amplified. DNA from the phages was isolated and sequenced to obtain the genetic information encoding for the displayed peptides. Analysis of over 30 independent clones provided only three different peptidesequences:AG3,AG4 and AG5 (table I) of these three" peptides, AG4 was the predominant sequence present within the sequenced clones. The silver-binding peptides do indicate a preferential enrichment of praline and hydrox3'1-containing amino acid residues, and there appears to be positional conservation of some of the amino acid residues. **We confirmed the binding of the phage clones to silver surfaces**

using indirect immunofluorescence (Supplementary Information Fig. S1). (Emphasis added.)

Applicants state that none of the applied references teach "associating a biomolecule with the identified peptide" or "wherein a nanocode is bound to the biomolecule" as recited in new claim 40.

In reply, see the restriction requirement above withdrawing the newly added distinct method of claim 40.

Claims 1, 4-7 and 18, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al (Science).

Lee discloses at page 893, Fig. 1 a method of identifying peptide by contacting a phage library with a surface comprising a target with a geometrical shape. See the entire article.

Since applicants have not responded to this rejection hence, it is believed that applicants are acquiescing therewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1, 4-7, 10-12, 15-16, 18 and 37-39, as amended and added, are rejected under 35 U.S.C. 103(a) as being unpatentable

over any one of Naik or Belcher or Lee in view of Puntes (Science) for reasons of record as repeated below.

Each of Naik, Belcher and Lee is discussed above. Each of these references does not disclose a surface comprising a surfactant. However Puntes teaches at page 2115 up to page 2117 the use of surfactant. Puentes teaches that the use of surfactant results in the preparation of wide range of shapes including rod, teardrops, and tetrapods and branched tetrapods. The shapes can be made simply by varying surfactant compositions as learned from the prototypical CdSe system. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a surfactant in the surface of e.g., Naik as taught by Puntes. The advantages taught by Puntes in the use of surfactant composition would provide the motivation to one having ordinary skill in the art at the time the invention was made.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Naik or Belcher or Lee as applied to claims 1, 4-7, 10-12, 15-16, 18 and 37-39 above, and further in view of Freeman et al (Science).

Naik or Belcher or Lee does not disclose a surface with a Teflon as recited in claim 17. However, Freeman at page 1629 teaches a substrate comprising Teflon. Freeman discloses that

the Teflon is conventionally used as a substrate. The solution-based process taught by Freeman is extremely general encompassing numerous permutations of insulating and conducting substrates including Teflon. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use as a surface substrate, Teflon in the method of e.g., Naik as taught by Freeman. The different permutations that can be done to the conventional substrate as Teflon as taught by Freeman would provide the motivation to one having ordinary skill in the art, at the time the invention was made.

Response to Arguments

Applicants argue that none of the prior art teaches or suggests the newly amended claim 1. Prior to this invention, to the best of Applicants knowledge, nobody had developed or used a method of fabricating biosensors by identifying peptides that bind to a flat surface of the biosensor as recited in claim 1. Thus, no combination of the applied references would have rendered independent claim 1 or any of the claims that depend on independent claim 1 obvious to persons of ordinary skill in the art at the time of the invention. Further, new independent claim 40 includes, inter alia, the step of "associating a biomolecule with the identified peptide of step (g), wherein a

nanocode is bound to the biomolecule." This feature is neither taught nor suggested by any of the applied references. Thus, no combination of the applied references would have rendered independent claim 40 or any of the claims that depend on independent claim 40 obvious to persons of ordinary skill in the art at the time of the invention.

In reply, the response above is incorporated herein since applicants merely presented the same arguments.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639